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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,256	09/13/2005	Angus Moodycliffe	112843-066	3290

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
12/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATENTS@BELLBOYD.COM

Office Action Summary	Application No.	Applicant(s)	
	10/525,256	MOODYCLIFFE ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 25, 2007 has been entered.

Status of Claims

Currently, claims 1-3 and 6-8 are pending and under examination on the merits.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a composition comprising an RNAi oligonucleotide. The independent claims, claims 1 and 6, are drawn to compositions comprising an antisense RNA polynucleotide. However, the claimed "RNAi oligonucleotide" is conventionally used to refer to a double-stranded RNA molecule that mediates RNA interference in the biotechnology art.

Hence, it is ambiguous and inherently inconsistent that the claimed "RNA polynucleotide antisense to" a target sequence, which is inherently a single-stranded molecule, is also claimed to be a double-stranded "RNAi oligonucleotide", thereby rendering the claims indefinite.

With regard to the term "RNAi oligonucleotide", it was previously addressed that the specification does not provide any support for the claimed "RNAi oligonucleotide". Applicant has responded by pointing to page 10 of the specification, which states, "According to a preferred embodiment such a substance may be an DNA or a cRNA (RNA-interference)." Nowhere in the specification appears the claimed subject matter "RNAi oligonucleotide", nor is there a clear definition as to what is meant by the "RNAi oligonucleotide". The term "cRNA" in the art means complementary RNA derived from cDNA through RNA synthesis. In light of the claim dependency and the disclosed statement (lines 11-12 of page 10), the claimed "RNAi oligonucleotide" will be construed as a single-stranded complementary RNA for examination purpose.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims are drawn to compositions for "preventing" or "treating" epithelial tissue damage, wherein the compositions comprise a single-stranded RNA molecule that is antisense to the glucosylceramide synthase mRNA sequence.

As written, the claimed compositions must confer the therapeutic or pharmaceutical properties of either "preventing" or "treating" any type of epithelial tissue damage. As such, the claimed compositions must be enabled for *in vivo* use for the claimed preventative or treatment effect.

Applicant's argument filed on October 25, 2007 are fully considered but they are not persuasive because applicant relies only on the "background" information that blocking endogenous CD_{1d} function in epithelial cells has been shown to prevent detrimental effect of

stress/skin damage. As pointed out in the prior Office action dated July 26, 2007, the specification contains no support for the claimed compositions comprising a polynucleotide antisense to the glucosylceramide synthase mRNA, let alone such compositions that treat or prevent epithelial tissue damage. In other words, the specification is silent about any enabling disclosure pertaining to the claimed compositions. Further, it was previously stated that the claimed target gene appears only on page 10 throughout the entire disclosure of the specification. In addressing this issue, applicant contends, "the specification clearly teaches that epithelial cell homeostasis can be maintained through the regulation of ceramides and glucosylceramides." Applicant's contention that the specification "clearly" teaches the regulatory role of glucosylceramides in epithelial cell homeostasis bears no relevance to the claimed antisense polynucleotide targeted to the glucosylcermaide synthase mRNA, which prevents or treats epithelial tissue damage for the following reasons:

First, the glucosylceramides and the claimed glucosylceramide synthase are two different genes/proteins. They are encoded by different genetic/amino acid codes.

Second, neither the instant specification nor the state of the prior art teaches that expression of glucosylceramide synthase is associated with epithelial tissue damage.

Third, it is unclear how the alleged regulatory role of glucosylceramides in maintaining epithelial cell "homeostatsis" is related to preventing/treating epithelial "damage" by silencing the clamed glucosylceramide synthase expression.

Fourth, page 10, lines 15-19 describe that reducing glucosylceramide synthase mRNA by an antisense polynucleotide turns down the signal to epithelial cells to proliferate. It is unclear

how reducing epithelial cell proliferation is related to treating/preventing epithelial tissue damage as claimed in the instant case.

Again, applicant's attention is directed to the complete lack of working examples for the claimed compositions. As stated in the previous Office action, the state of the gene therapy art remains highly unpredictable and the success or efficacy of any therapeutic nucleic-acid based composition widely varies case by case. As such, without working examples/guidance/directions commensurate in scope with the claimed invention, one of ordinary skill in the art cannot make the claimed compositions and use them to treat or prevent epithelial tissue damage unless the person performs undue experimentation.

In light of the reasons stated above, the specification fails to comply with the enablement requirement.

Claims 3 and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are drawn to compositions comprising an "RNAi" oligonucleotide. The term "RNAi" conventionally refers to a double-stranded short interfering RNA molecule in the biotechnology art. Although the specification contains the word "RNA interference", nowhere in the specification is it shown that the inventors contemplated making compositions comprising double-stranded RNAi molecules at the time the application was originally filed. Especially, the

word "RNA interference" was used to refer to complementary RNA (cRNA) in the instant application. As such, the mere reference of "RNA interference" in the specification does not provide support for the claimed "RNAi oligonucleotide", which is not a single-stranded complementary RNA, but a double-stranded RNA. Furthermore, the specification is devoid of the claimed word "RNAi oligonucleotide" and it provides no definition for the claimed substance. Since the claimed substance is not adequately described in the specification as originally filed, and since the passages pointed out by applicant alleging that the claimed "RNAi oligonucleotide" is fully supported by the disclosure of the specification do not appear to comply with the written description requirement, the claims comprising "RNAi oligonucleotide" introduce new matter, which was not disclosed in the specification as originally filed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner
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